The Claims Are Enabled Under 35 U.S.C. § 112, First Paragraph

Claims 1 and 11-17 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Specifically, the Examiner contends that:

> It is the first required screening with candidate host cell proteins and candidate viral proteins that is not adequately enabled because it essentially requires the skilled artisan to test all host cell proteins against all viral proteins and all viral proteins against all host proteins without sufficient guidance, and little predictability in the art, as to what host or viral proteins to test. Office Action, page 4).

The Examiner further asserts that the teachings of the specification amount to no more than:

> ...leaving the skilled artisan with the equivalent of a hunting license to go forth and look for additional appropriate protein-protein interactions..." (Office Action, page 4).

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. U.S. v. Telectronics, Inc. 857 F.2d 778, 8 USPQ 2d 1217 (Fed. Cir. 1988). Enablement is not precluded even if some experimentation is necessary. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986). The need for some experimentation does not render the claimed invention unpatentable under 35 U.S.C. § 112. This is so even if the amount of experimentation required is laborious. In re Wands 858 F.2d 731 (Fed. Cir. 1988).

In essence, the Examiner contends that the teachings of the specification do not enable the full scope of the claims. However, Applicants have made a pioneering invention of identifying viral protein/non-receptor-host cell protein interactions as targets for screening for antiviral compounds. Applicants' contribution to the art, *inter alia*, is the directing of the powerful technology of screening for protein-protein interactions toward the identification of the useful, novel targets of viral protein/non-receptor-host cell protein complexes. Furthermore, Applicants have described in detail methods that enable one of skill in the art to carry out the claimed invention across the full scope of the claims, using, at most, routine experimentation. Thus, Applicants have enabled and are entitled to the full scope of the claims.

In contrast to the Examiner's assertion, the specification provides specific examples in which the interactions of a number of viral and host cell proteins have been identified (Sections 6 and 7). Specifically, seven different host cell proteins are listed in Table I, at page 15 of the specification, which interact with either of two different viral proteins (influenza virus NP or NS1 proteins). The specification also describes a variety of other viruses and viral proteins that can be used to identify interactions with host cell proteins (page 8, line 4 to page 9, line 23).

Furthermore, the specification describes in detail methods that are readily applicable to identifying the protein-protein interactions specified in the claims (page 9, lines 12-30). In particular, the yeast interactive trap

(i.e., two-hybrid) system is described in detail at page 9, lines 23-30; and in Sections 6.1 and 7.1).

Applicants note, in this regard, that the specification describes in detail, for example, HeLa cell cDNA libraries that can be used to identify host cell proteins, including libraries that were commercially available at the filing date of the instant application (page 34, line 31 to page 35, line 3). The specification also describes in detail the construction of the second key component of the two-hybrid system: the viral protein-LexA fusion vector. The construction of this vector, which is exemplified for influenza virus NP and NS1, can be readily applied, in accordance with the teachings of the specification, to various other well know viral proteins.

Indeed, many various viral genes, including those described in the instant specification, had been well-characterized prior to the filing date of the instant application. Viral genetics, including viral molecular genetics, is one of the most well-studied areas of molecular biology. Applicants respectfully direct the Examiner's attention to Exhibit A, hereto, which contains selected passages from the basic virology text book, Fundamental Virology, Fields et al., eds. (Raven Press, 2nd ed. 1991). The pages from Fields et al. contained in Exhibit A clearly demonstrate that the genetic organization of a large number of viral genomes had been well characterized long before the filing date of the instant application. Thus, a person of ordinary skill in the art would be able to select various

viral genes appropriate for use in detecting interactions with non-receptor host cell proteins, in accordance with the invention, without undue experimentation.

In fact, since the filing date of the instant application, many viral protein-host cell protein interactions have been identified in accordance with the methods that are described in the specification using, for example, the two-hybrid system. Applicants respectfully direct the Examiner's attention to the following two references, each of which is attached hereto as exhibits as follows:

Exhibit B:	Donzeau *et al.*, 1997, J. Virol. 71: 2628-2635;
Exhibit C:	Huang *et al.*, 1996, J. Virol. 70: 5582-5591.

Exhibits B and C are but two of the many examples of reports published after the filing date of the instant application that describe the identification of protein-protein interactions, including, in particular, viral/host cell protein interactions, using the two-hybrid system described in detail in the instant application.

Thus, in contrast to the Examiner's assertion, there is <u>not</u> a high level of unpredictability in the art. In fact, the high level of <u>predictability</u> is evidenced by reports in the art published subsequent to the filing date of the instant application.

Moreover, once such protein-protein interactions have been identified, it would require only routine experimentation to determine the appropriate conditions to allow for detection

of the formation of complexes, in accordance with the claimed methods, between such proteins which necessarily form complexes in the two-hybrid system.

Therefore, in light of the specific examples of protein-protein interactions described in the specification, the detailed teachings in the specification for identifying such protein-protein interactions between other viral and host cell proteins, as well as the general level of skill in the art, the specification in no way amounts to a mere "hunting license", but rather enables the full scope of the claims. Accordingly, Applicants respectfully request that the rejection of Claims 1 and 11-17 under § 112, first paragraph, be withdrawn.

The rejection of Claims 1-3 and 11-17 under both § 112, first paragraph, and § 112, second paragraph, with respect to the term "corresponding to the binding site" has been obviated by the amendment to the claims replacing this term, pursuant to the Examiner's suggestion.

The Claims Are Definite Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected Claims 1-3 and 11-17 under § 112, second paragraph for lack of definiteness with respect to the term "small organic molecule".

In contrast to the Examiner's assertion, Applicants respectfully contend that the term "small organic molecule" is definite, and has a clear and widely accepted meaning in the art. One of ordinary skill in the art would readily understand that the term "small organic molecule" refers to

those organic molecules that are smaller than macromolecules. "Macromolecule" also has a clear and widely accepted meaning in the art. In particular, a well-known medical dictionary defines "macromolecule" as "a molecule of colloidial size; *e.g.*, proteins, polynucleic acids, polysaccharides" (Stedman's Medical Dictionary, 26th edition, Williams and Wilkins (Baltimore: 1995), at page 1051, a copy of which is attached hereto as Exhibit D). Thus, the small organic molecules specified in the claims do not include such colloidal sized molecules as proteins (*e.g.*, antibodies). Therefore, the claims are definite. Accordingly, Applicants respectfully request that the rejection under § 112, second paragraph be withdrawn.

The Claims Are Novel Under 35 U.S.C. § 102

Claim 1 is rejected under 35 U.S.C. § 102(b) as being anticipated by Barik et al., 1992, Proc. Natl. Acad. Sci. USA 83: 6282-6286 ("Barik et al. (AD)"). According to the Examiner, Barik et al. (AD) discloses the phosphorylation of a viral protein phosphoprotein P of vesicular stomatitis virus (VSV) by a host cell protein casein kinase II. The Examiner contends that Barik et al. (AD) describes identifying compounds that inhibit the phosphorylation of phosphoprotein P by casein kinase II, and that such identification of inhibitory compounds is within the scope of Claim 1.

Applicants note, however, that the alleged teachings of Barik et al. (AD) to which the Examiner refers relate merely to the inhibition of enzyme activity. In contrast to

this alleged teaching, Claim 1 specifies detecting the formation and inhibition of a complex between two protein fragment binding partners. Barik et al. does not describe or otherwise suggest detecting the formation of a complex between the proteins described therein, much less detecting the inhibition of such complex formation as specified in Claim 1.

Thus, the alleged teachings of Barik et al. (AD) are not within the scope of Claim 1, nor would it be obvious to use the proteins described in Barik et al. (AD) in the assay claimed in Claim 1. Accordingly, Barik et al. (AD) neither anticipates, nor makes obvious, the assay of Claim 1. Therefore, Applicants respectfully request that the rejection of Claim 1 under § 102 be withdrawn.

CONCLUSION

Applicants respectfully request the entry of the foregoing amendments and remarks into the file of the above-captioned application. Applicants believe that each ground for rejection or objection has been successfully overcome or obviated and that the application is in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application is earnestly requested.

Respectfully submitted,

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